

S37-3 Saturated fatty acids, a naturally occurring ligand of TLR4

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Obese adipose tissue is markedly infiltrated by macrophages, which may play a role in the pathogenesis of obesity and obesity-related diseases. Using an *in vitro* co-culture system composed of adipocytes and macrophages, we have provided evidence that a paracrine loop involving saturated fatty acids and TNF α derived from adipocytes and macrophages, respectively, establishes a vicious cycle that aggravates inflammatory changes in obese adipose tissue. Interestingly, saturated fatty acids, which are released in large quantities from hypertrophied adipocytes via the macrophage-induced adipocyte lipolysis, serve as a naturally occurring ligand for TLR4, thereby inducing the inflammatory changes in obese adipose tissue. We also found that highly purified eicosapentaenoic acid (EPA), one of the representative n-3 polyunsaturated fatty acids (n-3PUFAs), is capable of antagonizing the saturated fatty acid-induced inflammatory changes in macrophages and inhibiting monocyte adhesion to endothelial cells, thereby explaining the anti-atherogenic effect of EPA. Recently, we have identified activating transcription factor 3, a stress-induced transcriptional repressor, as a target gene of the saturated fatty acids/TLR4/NF- κ B pathway and found that it may improve obesity-induced adipose tissue inflammation through the inhibition of saturated fatty acid-induced increase in pro-inflammatory cytokines in macrophages.

In this talk, we will discuss the pathophysiologic role of saturated fatty acids, a naturally occurring ligand for TLR4, in obesity and obesity-related diseases.